CLAIMS

1. A composition comprising a heterologous antigen linked to one or more non-primate hepadnavirus core antigen sequence that comprises a loop region.

2. The composition of Claim 1, wherein said heterologous antigen is inserted in said hepadnavirus core antigen.

3. The composition of Claim 2, wherein said insertion is inside said loop region.

4. The composition of Claim 2, wherein said insertion is outside said loop region.

5. The composition of Claim 1, wherein the C-terminal sequence of said hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids.

6. The composition of Claim 1, wherein said heterologous antigen comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

7. The composition of Claim 1, wherein said hepadnavirus core antigen sequence comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

8. The composition of Claim 1, wherein said heterologous antigen comprises at least one B cell epitope.

9. The composition of Claim 1, wherein said heterologous antigen comprises at least one T cell epitope.

10. The composition of Claim 9, wherein said heterologous antigen comprises at least one CD4+ T cell epitope.

11. The composition of Claim 9, wherein said CD4+ T cell epitope comprises one or more sequence chosen from SEQ ID NOs:239-256.

12. The composition of Claim 1, wherein said composition further comprises at least one immune enhancer sequence linked to one or more of said heterologous antigen and to said hepadnavirus core antigen sequence.

13. The composition of Claim 1, wherein said composition further comprises one or more of 1) wild type non-primate hepadnavirus core antigen, and 2) modified non-primate hepadnavirus core antigen lacking a heterologous antigen.

14. The composition of Claim 1, wherein said non-primate hepadnavirus core antigen sequence is a rodent hepadnavirus core antigen sequence.

15. The composition of Claim 14, wherein said rodent hepadnavirus core antigen sequence is chosen from one or more of woodchuck hepatitis virus core antigen, arctic ground squirrel hepatitis virus core antigen, and ground squirrel hepatitis virus core antigen.

16. The composition of Claim 1, wherein said heterologous antigen is inserted inside said loop region.

17. The composition of Claim 16, wherein said position inside said loop region is chosen from amino acid residues 77, 78, 81, and 82.

18. The composition of Claim 16, wherein said position inside said loop region is at amino acid residue 76.

19. The composition of Claim 14, wherein said heterologous antigen is inserted at a position outside said loop region.

20. The composition of Claim 19, wherein said position outside said loop region is chosen from amino acid residues 71, 72, 73, 74, 75, 83, 84, 85, 92, N-terminal and C-terminal.

21. The composition of Claim 19, wherein said position outside said loop region is at amino acid residue 44.

22. The composition of Claim 14, wherein said heterologous antigen is inserted at a position inside said loop region and in a position outside said loop region.

23. The composition of Claim 14, wherein the C-terminal sequence of said rodent hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids.

24. The composition of Claim23, wherein said 1 to 100 amino acids is chosen from R, C, K, A, RRC, and SEQ ID NOs:2-20, 22-36, 42-56, 153, 155, 157, 159, 161,163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183-238.

25. The composition of Claim 24, wherein said hepadnavirus core antigen sequence is a woodchuck hepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said woodchuck hepadnavirus core antigen.

26. The composition of Claim 24, wherein said hepadnavirus core antigen sequence is a ground squirrel hepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said ground squirrel hepadnavirus core antigen.

27. The composition of Claim 24, wherein said hepadnavirus core antigen sequence is arctic ground squirrel hepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said arctic ground squirrel hepadnavirus core antigen.

28. The composition of Claim 14, wherein said heterologous antigen comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

29. The composition of Claim 14, wherein said hepadnavirus core antigen sequence comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

30. The composition of Claim 14, wherein said heterologous antigen comprises at least one B cell epitope.

31. The composition of Claim 14, wherein said heterologous antigen comprises at least one T cell epitope.

32. The composition of Claim 14, wherein said composition further comprises at least one immune enhancer sequence linked to one or more of said heterologous antigen and to said hepadnavirus core antigen sequence.

33. The composition of Claim 14, wherein said composition further comprises one or more of 1) wild type rodent hepadnavirus core antigen, and 2) modified rodent hepadnavirus core antigen lacking a heterologous antigen.

34. The composition of Claim 1, wherein said non-primate hepadnavirus core antigen sequence is an avihepadnavirus core antigen sequence.

35. The composition of Claim 34, wherein said avihepadnavirus core antigen sequence is chosen from one or more of duck avihepadnavirus core antigen sequence, Ross' goose avihepadnavirus core antigen sequence, heron avihepadnavirus core antigen sequence, Sheldgoose avihepadnavirus core antigen sequence, and stork avihepadnavirus core antigen sequence.

36. The composition of Claim 34, wherein said heterologous antigen is inserted at a position within said loop region.

37. The composition of Claim 36, wherein said position within said loop region is chosen from amino acid residues 91, 92, 93, 96, and 97.

38. The composition of Claim 34, wherein said heterologous antigen is inserted at a position outside of said loop region.

39. The composition of Claim 38, wherein said position outside said loop region is chosen from amino acid residues 86, 87, 88, 89, 90, 98, 99, 131, 138, N-terminal and C-terminal.

40. The composition of Claim 38, wherein said position outside said loop region is at amino acid residue 40.

41. The composition of Claim 34, wherein said heterologous antigen is inserted at a position within said loop region and in a position outside said loop region.

42. The composition of Claim 34, wherein the C-terminal sequence of said avihepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids.

43. The composition of Claim 34, wherein said 1 to 100 amino acids is chosen from R, C, K, A, RRC, and SEQ ID NOs:2-20, 22-36, 42-56, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183-238.

44. The composition of Claim 43, wherein said avihepadnavirus core antigen sequence is a duck avihepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said duck avihepadnavirus core antigen.

45. The composition of Claim 43, wherein said avihepadnavirus core antigen sequence is a Ross' goose avihepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said Ross' goose avihepadnavirus core antigen.

46. The composition of Claim 43, wherein said avihepadnavirus core antigen sequence is a heron avihepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said heron avihepadnavirus core antigen.

47. The composition of Claim 43, wherein said avihepadnavirus core antigen sequence is a Sheldgoose avihepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said Sheldgoose avihepadnavirus core antigen.

48. The composition of Claim 43, wherein said avihepadnavirus core antigen sequence is a stork avihepadnavirus core antigen sequence, and said 1 to 100 amino acids does not consist of the wild type C-terminal sequence of said stork avihepadnavirus core antigen.

49. The composition of Claim 34, wherein said heterologous antigen comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

50. The composition of Claim 34, wherein said hepadnavirus core antigen sequence comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

51. The composition of Claim 34, wherein said heterologous antigen comprises at least one B cell epitope.

52. The composition of Claim 34, wherein said heterologous antigen comprises at least one T cell epitope.

53. The composition of Claim 34, wherein said composition further comprises at least one immune enhancer sequence linked to one or more of said heterologous antigen and to said hepadnavirus core antigen sequence.

54. The composition of Claim 34, wherein said composition further comprises one or more of 1) wild type avihepadnavirus core antigen, and 2) modified avihepadnavirus core antigen lacking a heterologous antigen.

55. The composition of Claim 34, wherein said avihepadnavirus core antigen sequence comprises a deletion of at least a portion of the loop region.

56. The composition of Claim 55, wherein said deletion comprises a deletion of from 1 to 40 amino acids of said loop region.

57. The composition of Claim 55, wherein said deletion comprises a deletion of said loop region.

58. A composition comprising a heterologous antigen linked to one or more primate hepadnavirus core antigen sequence that comprises a loop region, wherein the C-terminal sequence of the hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids, and wherein said 1 to 100 amino acids does not consist of cysteine or of the wild type C-terminal sequence of said hepadnavirus core antigen.

59. The composition of Claim 58, wherein said 1 to 100 amino acids is chosen from R, K, A, RRC, and SEQ ID NOs:2-20, 22-36, 43-56, 153, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183-238.

60. The composition of Claim 58, wherein said heterologous antigen is inserted in said hepadnavirus core antigen.

61. The composition of Claim 60, wherein said insertion is inside said loop region.

62. The composition of Claim 60, wherein said insertion is outside said loop region.

63. The composition of Claim 58, wherein said heterologous antigen comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

64. The composition of Claim 58, wherein said hepadnavirus core antigen sequence comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

65. The composition of Claim 58, wherein said heterologous antigen comprises at least one B cell epitope.

66. The composition of Claim 58, wherein said heterologous antigen comprises at least one T cell epitope.

67. The composition of Claim 58, wherein said composition further comprises at least one immune enhancer sequence linked to one or more of said heterologous antigen and to said hepadnavirus core antigen sequence.

68. The composition of Claim 58, wherein said composition further comprises one or more of 1) wild type primate hepadnavirus core antigen, and 2) modified primate hepadnavirus core antigen lacking a heterologous antigen.

69. The composition of Claim 58, wherein said primate hepadnavirus core antigen sequence is a human hepatitis B virus core antigen sequence.

70. The composition of Claim 69, wherein said human hepatitis B virus core antigen sequence is chosen from one or more of SEQ ID NOS:41, and 109-114.

71. The composition of Claim 69, wherein said heterologous antigen is inserted inside said loop region.

72. The composition of Claim 71, wherein said position inside said loop region is chosen from amino acid residues 77, 78, 81, and 82.

73. The composition of Claim 71, wherein said position inside said loop region is at amino acid residue 76.

74. The composition of Claim 69, wherein said heterologous antigen is inserted at a position outside said loop region.

75. The composition of Claim 74, wherein said position outside said loop region is chosen from amino acid residues 71, 72, 73, 74, 75, 83, 84, 85, 92, N-terminal and C-terminal.

76. The composition of Claim 74, wherein said position outside said loop region is at amino acid residue 44.

77. The composition of Claim 69, wherein said heterologous antigen is inserted at a position inside said loop region and in a position outside said loop region.

78. The composition of Claim 69, wherein said heterologous antigen comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

79. The composition of Claim 69, wherein said hepadnavirus core antigen sequence comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

80. The composition of Claim 69, wherein said heterologous antigen comprises at least one B cell epitope.

81. The composition of Claim 69, wherein said heterologous antigen comprises at least one T cell epitope.

82. The composition of Claim 69, wherein said composition further comprises at least one immune enhancer sequence linked to one or more of said heterologous antigen and to said hepadnavirus core antigen sequence.

83. The composition of Claim 69, wherein said composition further comprises one or more of 1) wild type human hepatitis B virus core antigen, and 2) modified human hepatitis B virus core antigen lacking a heterologous antigen.

84. The composition of Claim 58, wherein said primate hepadnavirus core antigen sequence is a non-human primate hepadnavirus core antigen sequence.

85. The composition of Claim 84, wherein said non-human primate hepadnavirus core antigen sequence is chosen from one or more of chimpanzee hepatitis B virus, gibbon hepatitis B virus, orangutan hepatitis virus, and woolly monkey hepatitis virus.

86. The composition of Claim 84, wherein said heterologous antigen is inserted at a position within said loop region.

87. The composition of Claim 86, wherein said position within said loop region is chosen from amino acid residues 77, 78, 81, and 82.

88. The composition of Claim 86, wherein said position within said loop region is at amino acid residue 76.

89. The composition of Claim 84, wherein said heterologous antigen is inserted at a position outside of said loop region.

90. The composition of Claim 89, wherein said position outside said loop region is chosen from amino acid residues 71, 72, 73, 74, 75, 83, 84, 85, 92, N-terminal and C-terminal.

91. The composition of Claim 89, wherein said position outside said loop region is at amino acid residue 44.

92. The composition of Claim 84, wherein said heterologous antigen is inserted at a position within said loop region and in a position outside said loop region.

93. The composition of Claim 84, wherein the C-terminal sequence of said non-human primate hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids.

94. The composition of Claim 93, wherein said 1 to 100 amino acids is chosen from R, K, A, RRC, and SEQ ID NOs:2-20, 22-36, 43-56, 153, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183-238.

95. The composition of Claim 84, wherein said heterologous antigen comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

96. The composition of Claim 84, wherein said hepadnavirus core antigen sequence comprises one or more of 1) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid, and 2) insertion of at least one acidic amino acid compared to the wild type hepadnavirus core antigen sequence.

97. The composition of Claim 84, wherein said heterologous antigen comprises at least one B cell epitope.

98. The composition of Claim 84, wherein said heterologous antigen comprises at least one T cell epitope.

99. The composition of Claim 84, wherein said composition further comprises at least one immune enhancer sequence linked to one or more of said heterologous antigen and to said hepadnavirus core antigen sequence.

100. The composition of Claim 84, wherein said composition further comprises one or more of 1) wild type non-human primate hepadnavirus core antigen, and 2) modified non-human primate hepadnavirus core antigen lacking a heterologous antigen.

101. A composition comprising one or more non-primate hepadnavirus core antigen sequence that comprises a loop region, wherein the C-terminal sequence of the hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids.

102. A composition comprising one or more primate hepadnavirus core antigen sequence that comprises a loop region, wherein the C-terminal sequence of the hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids, and wherein said 1 to 100 amino acids does not consist of cysteine or of the wild type C-terminal sequence of said hepadnavirus core antigen.

103. A nucleic acid sequence encoding one or more polypeptide composition of any of Claims 1-102.

104. An expression vector comprising one or more of the nucleic acid sequences of Claim 103.

105. A cell comprising one or more nucleic acid sequence of Claim 103.

106. A vaccine comprising one or more of (a) polypeptide composition of any of Claims 1-102, and (b) nucleic acid sequence of Claim 103.

107. A method for modifying a non-primate hepadnavirus core antigen, comprising:

a) providing:

i) a non-primate hepadnavirus core antigen comprising a loop region; and

ii) antigen that is heterologous to said non-primate hepadnavirus; and

b) inserting said antigen in said non-primate hepadnavirus core antigen.

108. The method of Claim 107, wherein said method further comprises determining antigenicity in vitro of the non-primate hepadnavirus core antigen produced by said method.

109. The method of Claim 107, wherein said method further comprises determining immunogenicity, in vivo in an animal, of the non-primate hepadnavirus core antigen produced by said method.

110. The method of Claim 109, wherein said mammal is chosen from mouse, non-human primate, and human.

111. The method of Claim 107, wherein said non-primate hepadnavirus is a rodent hepadnavirus.

112. The method of Claim 111, wherein said rodent hepadnavirus is chosen from arctic ground squirrel hepatitis virus (AGSHV), ground squirrel hepatitis virus (GSHV), and woodchuck hepatitis virus (WHV).

113. The method of Claim 112, wherein said arctic ground squirrel hepatitis virus (AGSHV) core antigen comprises SEQ ID NO:102.

114. The method of Claim 113, wherein said arctic ground squirrel hepatitis virus (AGSHV) core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:127.

115. The method of Claim 112, wherein said ground squirrel hepatitis virus (GSHV) core antigen comprises one or more of SEQ ID NO:21 and 108.

116. The method of Claim 115, wherein said ground squirrel hepatitis virus (GSHV) core antigen is encoded by a nucleic acid sequence comprising one or more of SEQ ID NO:39 and 128.

117. The method of Claim 112, wherein said woodchuck hepatitis virus (WHV) core antigen comprises one or more of SEQ ID NO:1, and 103-107.

118. The method of Claim 117, wherein said woodchuck hepatitis virus (WHV) core antigen is encoded by a nucleic acid sequence comprising one or more of SEQ ID NOs:37 and 129-133.

119. The method of Claim 107, wherein said non-primate hepadnavirus is an avihepadnavirus.

120. The method of Claim 119, wherein said avihepadnavirus is chosen from Ross' goose hepatitis virus, heron hepatitis virus, duck hepatitis virus, sheldgoose hepatitis virus, and stork hepatitis virus.

121. The method of Claim 120, wherein said Ross' goose hepatitis virus core antigen comprises SEQ ID NO:125.

122. The method of Claim 121, wherein said Ross' goose hepatitis virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:143.

123. The method of Claim 120, wherein said heron hepatitis virus core antigen comprises SEQ ID NO:126.

124. The method of Claim 123, wherein said heron hepatitis virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:144.

125. The method of Claim 120, wherein said duck hepatitis virus core antigen comprises one or more of SEQ ID NO:119-124.

126. The method of Claim 125, wherein said duck hepatitis virus core antigen is encoded by a nucleic acid sequence comprising one or more of SEQ ID NOs:145-150.

127. The method of Claim 120, wherein said sheldgoose hepatitis virus core antigen comprises SEQ ID NO:151.

128. The method of Claim 127, wherein said sheldgoose hepatitis virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:124.

129. The method of Claim 120, wherein said stork hepatitis virus core antigen comprises SEQ ID NO:152.

130. The method of Claim 129, wherein said stork hepatitis virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:126.

131. The method of Claim 119, wherein said inserting of said antigen is inside said loop region.

132. The method of Claim 119, wherein said inserting of said antigen is outside said loop region.

133. The method of Claim 119, wherein further comprises c) replacing the C-terminal sequence of the hepadnavirus core antigen sequence with from 1 to 100 amino acids, wherein steps b) and c) are carried out in any order or are concomitant.

134. The method of Claim 119, wherein said antigen comprises a polypeptide, and wherein said method further comprises c) modifying one or more of said non-primate hepadnavirus core antigen and said heterologous antigen, by one or more of (i) inserting at least one acidic amino acid, and (ii) substituting at least one amino acid that is not an acidic amino acid with one or more acidic amino acid, wherein steps b) and c) are carried out in any order or are concomitant.

135. The method of Claim 134, wherein the modified heterologous antigen comprises a sequence chosen from one or more of SEQ ID no: 73, 74, 75, 77, 78, 79, 80, 81, 83, 98, 99, 100, and 101.

136. The method of Claim 119, wherein the method further comprises c) linking at least one immune enhancer sequence to one or more of said heterologous antigen and to said non-primate hepadnavirus core antigen sequence, and wherein steps b) and c) are carried out in any order or are concomitant.

137. The method of Claim 119, wherein said antigen comprises one or more of SEQ ID NOs:70-92.

138. The method of Claim 119, wherein said hepadnavirus is an avihepadnavirus, and said method further comprises c) deleting at least a portion of the loop region in said avihepadnavirus core antigen, and wherein steps b) and c) are carried out in any order or are concomitant.

139. The method of Claim 138, wherein said deleting comprises deleting a portion of said loop region.

140. The method of Claim 138, wherein said deleting comprises deleting said loop region.

141. A method for modifying a primate hepadnavirus core antigen, comprising:

a) providing:

i) a primate hepadnavirus core antigen comprising a loop region; and

ii) antigen that is heterologous to said primate hepadnavirus;

b) inserting said antigen in said primate hepadnavirus core antigen; and

c) replacing the C-terminal sequence of the hepadnavirus core antigen sequence with from 1 to 100 amino acids, wherein said 1 to 100 amino acids does not consist of cysteine or of the wild type C-terminal sequence of said hepadnavirus core antigen, wherein steps b) and c) are carried out in any order or are concomitant.

142. The method of Claim 141, wherein said method further comprises determining antigenicity in vitro of the primate hepadnavirus core antigen produced by said method.

143. The method of Claim 141, wherein said method further comprising determining immunogenicity, in vivo in an animal, of the primate hepadnavirus core antigen produced by said method.

144. The method of Claim 143, wherein said mammal is chosen from mouse, non-human primate, and human.

145. The method of Claim 141, wherein said primate hepadnavirus is a human hepatitis B virus.

146. The method of Claim 145, wherein said human hepatitis B virus core antigen comprises one or more of SEQ ID NOs:41, 109-114.

147. The method of Claim 146, wherein said human hepatitis B virus core antigen is encoded by a nucleic acid sequence comprising one or more of SEQ ID NOs:57 and 138-142.

148. The method of Claim 141, wherein said primate hepadnavirus is a non-human primate hepadnavirus.

149. The method of Claim 148, wherein said non-human primate hepadnavirus is chosen from orangutan hepatitis virus, woolly monkey hepatitis virus, gibbon hepatitis B virus, and chimpanzee hepatitis B virus.

150. The method of Claim 149, wherein said orangutan hepatitis virus core antigen comprises SEQ ID NO:117.

151. The method of Claim 150, wherein said orangutan hepatitis virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:134.

152. The method of Claim 149, wherein said woolly monkey hepatitis virus core antigen comprises SEQ ID NO:118.

153. The method of Claim 152, wherein said woolly monkey hepatitis virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:135.

154. The method of Claim 152, wherein said gibbon hepatitis B virus core antigen comprises SEQ ID NO:116.

155. The method of Claim 154, wherein said gibbon hepatitis B virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:136.

156. The method of Claim 152, wherein said chimpanzee hepatitis B virus core antigen comprises SEQ ID NO:115.

157. The method of Claim 156, wherein said chimpanzee hepatitis B virus core antigen is encoded by a nucleic acid sequence comprising SEQ ID NO:137.

158. The method of Claim 141, wherein said inserting of said antigen is inside said loop region.

159. The method of Claim 141, wherein said inserting of said antigen is outside said loop region.

160. The method of Claim 141, wherein said antigen comprises a polypeptide, and wherein said method further comprises c) modifying one or more of said primate hepadnavirus core antigen and said heterologous antigen, by one or more of (i) inserting at least one acidic amino acid, and (ii) substituting at least one amino acid that is not an acidic amino acid with one or more acidic amino acid, and wherein steps b) and c) are carried out in any order or are concomitant.

161. The method of Claim 160, wherein the modified heterologous antigen comprises a sequence chosen from one or more of SEQ ID NOs: 73, 74, 75, 77, 78, 79, 80, 81, 83, 98, 99, 100, and 101.

162. The method of Claim 141, wherein further comprises c) linking at least one immune enhancer sequence to one or more of said heterologous antigen and to said primate hepadnavirus core antigen sequence, wherein steps b) and c) are carried out in any order or are concomitant.

163. The method of Claim 141, wherein said antigen comprises one or more of SEQ ID NOs:70-92.

164. A method for producing an immunogenic composition, comprising:

a) providing:

i) a non-primate hepadnavirus core antigen sequence comprising a loop region; and

ii) an antigen that is heterologous to said hepadnavirus core antigen;

b) altering at least one of said heterologous antigen and said hepadnavirus core antigen with a modification chosen from one or more of:

i) insertion of at least one acidic amino acid; and

ii) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid;

c) producing a modified hepadnavirus core antigen by inserting one or more of:

i) the altered heterologous antigen of step b into said hepadnavirus core antigen of step a;

ii) the heterologous antigen of step a into the altered hepadnavirus core antigen of step b; and

iii) the altered heterologous antigen of step b into the altered hepadnavirus core antigen of step b; and

d) expressing said modified hepadnavirus core antigen under conditions suitable for producing hepadnavirus particles having a diameter of 25 to 35 nm, wherein steps b) and c) are in any order or are concomitant.

165. The method of Claim 164, wherein in the absence of said altering, expression of said modified hepadnavirus core antigen yields 25 fold less hepadnavirus particles than does expression of a wild type hepadnavirus core antigen.

166. The method of Claim 164, wherein said at least one acidic amino acid residue comprises (i) at least one aspartic acid residue, (ii) at least one glutamic acid residue, and (iii) at least one aspartic acid and at least one glutamic acid.

167. The method of Claim 164, wherein said insertion of acidic amino acid is in at least one position chosen from the N-terminus and the C-terminus of said heterologous antigen.

168. The method of Claim 164, wherein said substitution with acidic amino acid comprises replacement of at least one amino acid that is not an acidic amino acid of said heterologous antigen with at least one acidic amino acid residue.

169. The method of Claim 164, wherein said altering produces a modified heterologous antigen having an isoelectric point in the range of from 3.0 to 6.0.

170. A method for producing an immune response, comprising:

a) providing:

i) an animal; and

ii) a composition comprising one or more of:

1) a polypeptide comprising a non-primate hepadnavirus core antigen amino acid sequence linked to a heterologous antigen, wherein said hepadnavirus core antigen comprises a loop region, and

2) an expression vector encoding said polypeptide; and

b) administering said composition to said animal under conditions such that an immune response is generated to said heterologous antigen.

171. The method of Claim 170, wherein said immune response comprises one or more of lymphocyte proliferative response, cytokine response and antibody response.

172. The method of Claim 171, wherein said antibody response comprises production of IgG antibodies.

173. The method of Claim 172, wherein said IgG antibodies comprise autoantibody.

174. The method of Claim 170, wherein said non-primate hepadnavirus core antigen sequence is a rodent hepadnavirus core antigen sequence.

175. The method of Claim 170, wherein said non-primate hepadnavirus core antigen sequence is an avihepadnavirus core antigen sequence.

176. A method for producing an immune response, comprising:

a) providing:

i) an animal; and

ii) a composition comprising one or more of:

1) a polypeptide comprising a heterologous antigen linked to one or more primate hepadnavirus core antigen sequence that comprises a loop region, wherein the C-terminal sequence of the hepadnavirus core antigen sequence is replaced by from 1 to 100 amino acids, and wherein said 1 to 100 amino acids does not consist of cysteine or of the wild type C-terminal sequence of said hepadnavirus core antigen; and

2) an expression vector encoding said polypeptide; and

b) administering said composition to said animal under conditions such that an immune response is generated to said heterologous antigen.

177. The method of Claim 176, wherein said immune response comprises one or more of lymphocyte proliferative response, cytokine response and antibody response.

178. The method of Claim 177, wherein said antibody response comprises production of IgG antibodies.

179. The method of Claim 178, wherein said IgG antibodies comprise an autoantibody.

180. The method of Claim 176, wherein said primate hepadnavirus core antigen sequence is a human hepatitis B virus core antigen sequence.

181. The method of Claim 176, wherein said primate hepadnavirus core antigen sequence is a non-human primate hepadnavirus core antigen sequence.

182. A method for producing an immunogenic composition, comprising:

a) providing:

i) a primate hepadnavirus core antigen sequence comprising a loop region; and

ii) an antigen that is heterologous to said hepadnavirus core antigen;

b) altering at least one of said heterologous antigen and said hepadnavirus core antigen with a modification chosen from one or more of:

i) insertion of at least one acidic amino acid; and

ii) substitution of an amino acid that is not an acidic amino acid with at least one acidic amino acid;

c) producing a modified hepadnavirus core antigen by inserting one or more of:

i) the altered heterologous antigen of step b into said hepadnavirus core antigen of step a;

ii) the heterologous antigen of step a into the altered hepadnavirus core antigen of step b; and

iii) the altered heterologous antigen of step b into the altered hepadnavirus core antigen of step b; and

d) expressing said modified hepadnavirus core antigen under conditions suitable for producing hepadnavirus particles having a diameter of 25 to 35 nm, wherein steps b) and c) are in any order or are concomitant.

183. The method of Claim 182, wherein in the absence of said altering, expression of said modified hepadnavirus core antigen yields 25 fold less hepadnavirus particles than does expression of a wild type hepadnavirus core antigen.

184. The method of Claim 182, wherein said at least one acidic amino acid residue comprises one or more of at least one aspartic acid residue, and at least one glutamic acid residue.

185. The method of Claim 182, wherein said insertion of acidic amino acid is in at least one position chosen from the N-terminus and the C-terminus of said heterologous antigen.

186. The method of Claim 182, wherein said substitution with acidic amino acid comprises replacement of at least one amino acid that is not an acidic amino acid of said heterologous antigen with at least one acidic amino acid residue.

187. The method of Claim 182, wherein said altering produces a modified heterologous antigen having an isoelectric point in the range of from 3.0 to 6.0.